histone code of post-translational modifications and other properties of chromatin now recognized to be general features of eukaryotic biology. Other credits include the discovery of self-splicing RNA, the first sequencing of telomeric repeats and the discovery of telomerase. More recently, macronucleus differentiation by DNA elimination revealed a role for an RNAi pathway in heterochromatin formation. Further studies have described avoidance behavior, surface antigen variation and a stunning complexity of microtubule and membrane systems.

Why work with* Tetrahymena*? Robust methods for strain storage, gene targeting and designer genetic crosses have been developed, complementing the long-standing ease of cytology, micromanipulation and biochemistry. *Tetrahymena* entered the model organism pantheon with the recent sequencing and assembly of the macronucleus genome coordinated from The Institute for Genomic Research. Genome sequence, open reading frame predictions, EST sequences and gene indices are free online (http://www.tigr.org/tdb/euk/).

Where can I learn more? The *Tetrahymena* Genome Database (TGD) coordinated from Stanford University (http://www.ciliate.org/) contains a wealth of information, including ciliate literature compiled for text search by keyword or other features. For additional methods and discussion of many fascinating aspects of *Tetrahymena* and ciliate biology, we recommend: *The Molecular Biology of Ciliated Protozoa* (J.G. Gall, Editor, Academic Press, 1986); and *Methods in Cell Biology. Volume 62:* Tetrahymena thermophila (D.J. Asai and J.D. Forney, Editors, Academic Press, 2000).

[1]Department of Molecular and Cell Biology, University of California, Berkeley, California 94720–3204, USA. [2]Department of Biology, University of Rochester, Rochester, New York,14627, USA. E-mail: kcollins@berkeley.edu; goro@mail.rochester.edu

All phaged out

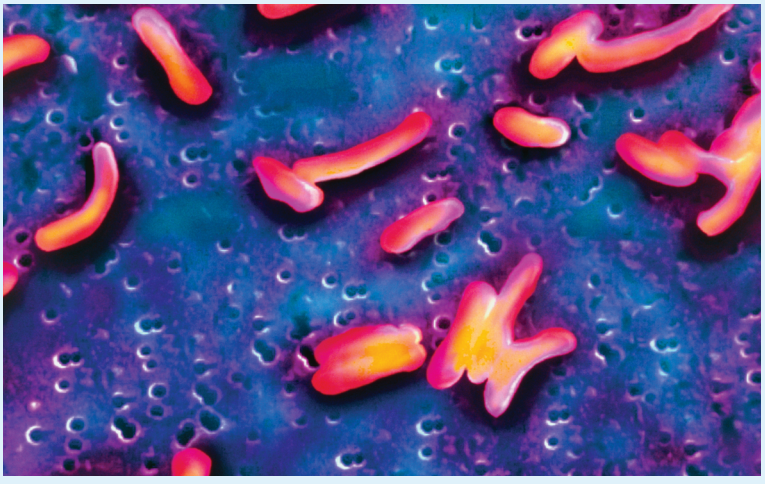
One of the puzzling aspects of devastating cholera outbreaks in areas where the disease is endemic is that they generally appear to fizzle out naturally. In Bangladesh, outbreaks usually occur twice a year, with the highest number of cases just after the summer monsoon and a somewhat smaller number of cases in the spring. It appears that a number of biological and physical factors may affect the survival and abundance of the disease-causing bacteria, *Vibrio cholerae.* But the disease is only carried by the strains O1 and O139 of the bacteria and researchers have puzzled how environmental factors might affect these strains.

Recent work has suggested that predation of *V. cholerae* O1 by bacteriophages may influence this seasonal pattern of epidemics, as it is known that this disease-causing strain is sensitive to a particular lytic bacteriophage, called JSF4. It has, however, been difficult for researchers to get quantitative, dynamic data on the presence of the toxic strain and bacteriophages both in the environment and in patients during the course of an epidemic.

But a team led by Shah Faruque at the International Centre for Diarrhoeal Disease Research in Dhaka, and John Mekalanos at Harvard Medical School in Boston now report a study in the Proceedings of the National Academy of Sciences (published online), describing a quantitative estimate of a pathogenic *V. cholerae* O1 and the lytic bacteriophage JSF4 in environmental water samples and from faeces of patients through the course of an epidemic in Dhaka last year.

The team exploited the fact that the toxigenic *V. cholerae* O1 causing recent epidemics is resistant to multiple antibiotics, including streptomycin. So the team tested for the presence of this strain in samples by selecting for it on culture plates containing streptomycin which would kill non-resistant strains of the bacteria. The team also used this system to monitor the changing prevalence of this strain in relation to that of the JSF4 lytic bacteriophage during the course of the epidemic.

The researchers tested the sensitivity of their assay to detect the pathogenic *V. cholerae* O1 amongst the many other non-pathogenic *V. cholerae* bacteria in their samples by comparing cultures on media containing or not containing streptomycin. Selection on streptomycin plates



Under pressure: The growth in numbers of disease-causing *Vibrio cholera* bacteria strains may be quickly followed by increased numbers of lytic bacteriophages that can drastically reduce their number in field situations. (Picture: Science Photo Library.)

revealed 141 of 339 samples contained *V. cholerae* O1 whereas only 60 samples were positive for *V. cholerae* O1 from plates without streptomycin, suggesting a much greater sensitivity in tracking the pathogen than in tests without using the antibiotic. This provided the researchers with greater accuracy in following the pathogen throughout the epidemic. As expected, the researchers found the number of patients suffering from cholera rose throughout the start of the epidemic before cases eventually declined. But they also found that the presence of the toxic bacteria and its lytic bacteriophage also varied considerably too throughout the epidemic.

The team found that the peak of the epidemic was preceded by high *V. cholerae* O1 levels in water samples from the environment to which patients were exposed, which was followed by high JSF4 phage levels as the epidemic ended.

The build-up to the peak detection of the JSF4 phage in the environment coincided with increasing excretion of it in the faeces of cholera patients. "These results suggest that patients towards the end of the epidemic ingested both JSF4 phage and the outbreak cholera strain," the authors say.

They suggest that phage amplification in patients infected by the disease at this stage may have contributed to increased phage abundance, decreasing the numbers of environmental *V. cholerae* O1 and, hence, the collapse of the epidemic. These results "may explain the self-limiting nature of seasonal cholera epidemics in Bangladesh," the authors report.

The authors also believe the evidence that phage may help control a major human bacterial disease could be put to clinical use. The work has "significant implications in devising cholera control measures by possible phage-mediated interventions," the authors say.

Primer

The optical structures of animal eyes

Michael F. Land

The ability to respond to light is common to many forms of life, but eyes themselves — structures that break up environmental light according to its direction of origin — are only found in animals. At its simplest, an eye might consist of a small number of light-responsive receptors in a pigmented pit, which shadows some receptors from light in one direction, and others from a different direction (Figure 1A). This definition distinguishes an eye from an organ with a single photoreceptor cell, which may indeed be directional because of screening pigment, but which does not allow for spatial vision — the simultaneous comparison of light intensities in different directions [1]. An alternative starting point for an eye would be for each receptor to have its own pigmented tube (Figure 2A), the assemblage forming a convex cushion. In these two proto-eye structures we have the beginnings of the two mutually exclusive ways of building an eye: the single-chambered range of eyes, often misleadingly called 'simple', and the compound eyes.

Although no eyes survive in fossils from the Precambrian (more than 550 million years ago) it seems certain that eyes like these were present from early in the evolution of the Bilateria [2], long before the Cambrian explosion. Simple pit eyes (Figure 1A) are still present in flatworms, annelid worms and molluscs, and in many larval eyes. Proto-compound eyes (Figure 2A) occur in ark clams and some tube-dwelling polychaetes, where they act as detectors of moving predators. Genetic, developmental and morphological evidence indicates that, from the earliest times, eyes had access to two different photoreceptor types: ciliary receptors, in which the photosensitive pigment is displayed on outgrowths of cilia, and rhabdomeric receptors, in

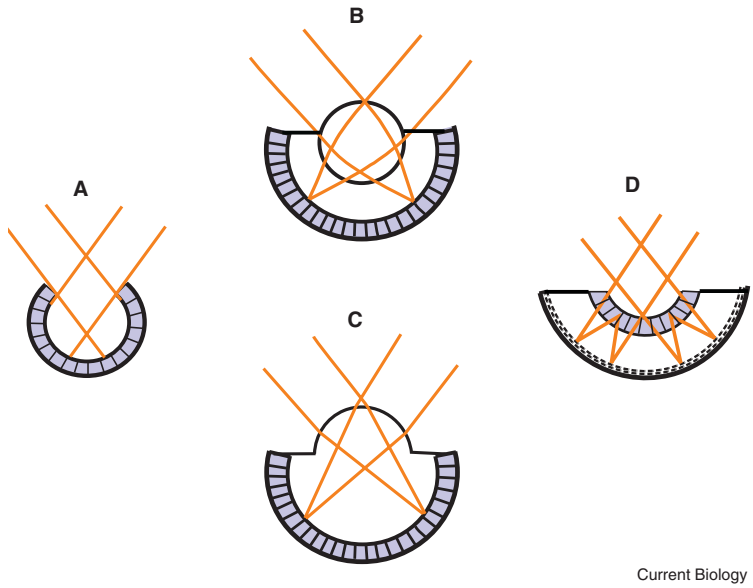


Figure 1. Single-chambered eyes.
(A) A simple pit eye, relying only on shadowing (platyhelminthes, annelids, molluscs and many larvae). (B) Spherical lens eye (fish, cephalopods and molluscs). (C) Eye with corneal optics (land vertebrates and spiders). (D) Eye imaging with a concave mirror (scallops and some crustaceans). Retinal structures are shown in purple. Rays show how light from distant points is imaged.